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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,461	03/27/2001	Benjamin D. Silverman	YOR920000779US2	1831
7590 04/03/2006 Ryan, Mason & Lewis, LLP 1300 Post Road, Suite 205 Fairfield, CT 06430			EXAMINER BORIN, MICHAEL L	
			ART UNIT 1631	PAPER NUMBER
DATE MAILED: 04/03/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

09/818,461

**Applicant(s)**

SILVERMAN, BENJAMIN D.

**Examiner**

Michael Borin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-43 is/are pending in the application.
- 4a) Of the above claim(s) 4, 7-21, 28-32, 36 and 39-43 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-3, 5, 6, 22-24, 26, 27, 33-35, 37, 38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

***DETAILED ACTION***

***Status of the claims***

1. Amendment filed 01/09/2006 is acknowledged. Claims 1-43 are pending. Claims 4,7-21,28-32,36,39-43 remain withdrawn from consideration. Claims 1-3,5,6,22-24,26,27,33-35,37,38 are under examination.

***Claim Rejections - 35 USC § 112, second paragraph.***

2. Claim 1, and claims dependent therefrom, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble. The preamble states that it is "a method for spatially profiling proteins", however, the claim recites a final step of "shifting the hydrophobicity distribution". While minor details are not required in method/process claims, at least the basic step must be recited in a positive, active fashion. The claim does not set forth the conditions when the determining/shifting of hydrophobicity distribution results in "spatially profiling proteins".

**Response to arguments**

Applicant's arguments have been considered but were not deemed persuasive for the following reasons. Applicant argues that the steps of determining hydrophobicity distribution agree back with preamble and that the steps as claimed "place a protein with mathematical basis for comparison". Thus, it seems that the method as claimed is directed to providing the "mathematical basis for comparison of proteins" rather than to "spatial profiling to describe three-dimensional structure" : the steps of spatial profiling. By the way of example, applicant points at p.9. As addressed previously, specification teaches on p. 4, last paragraph, that hydrophobicity distribution is merely a "value that indicates the degree to which a residue is attracted or repelled by water". Examiner reiterates that obtaining just a number characterizing a residue does not correspond to "spatial profiling", and thus maintains that the claim language fails to recite a final process step which agrees back with the preamble. While minor details are not required in method/process claims, at least the basic step must be recited in a positive, active fashion. The claim does not set forth the conditions when the determining/shifting of hydrophobicity distribution results in "spatially profiling proteins".

B. (NEW). Claim 1 is amended to recite "to describe three-dimensional structure". It is not clear what aspects of a three-dimensional structure are intended to be described. The only guidance in specification in this regard is that using the method allows to verify whether a protein, such as a man-made decoy protein, would have a globular structure. See, e.g., paragraphs [0009], [0024]. The specification, however, although providing particular examples, does not provide an explanation for ascertaining what

three-dimensional structures are intended to be described, and one of ordinary skills in the art would not be reasonably appraised of the scope of the invention.

***Claim Rejections - 35 U.S.C. § 101***

3. Claims 1-3,6,22-24,27,33-35,38 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The rejection is applied for the reasons of record and further in view of the following.

Applicant's arguments have been considered and are deemed to be persuasive-in-part. Rejection of claims 5,26,37 is withdrawn. With respect to the remaining claims, first, the argument presented on p. 16 of the response seems to be addressing whether the invention as claimed is directed to non-statutory subject matter. While Examiner disagrees with applicant's reasoning, such rejection is not currently on record.

Applicant further argues (p. 16, bottom) that specification on pages 4, 5 describes application of calculating of second-order hydrophobicity moments to determining whether a protein is globular. However, the claims currently being rejected are not directed to calculation of second-order moment of hydrophobicity.

Further, applicant argues that the "real world" utility of the invention is substantiation of predicted 3-dimensional protein structure from one-dimensional sequence data. While a need for such analysis is addressed in the art (as described in the cited part of the Background section) the instant method does not determine 3-dimensional protein structure; rather the method provides "the capability" of spatially

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profiling the hydrophobicity distribution of amino acid residues which can further be utilized in analysis of three-dimensional structure; i.e., further research steps are required for the method to have a demonstrated substantial utility. As stated in the rejection, the art, with respect to applying parameters of hydrophobicity, is unpredictable. The cited reference of Karplus teaches that :

Over the years, numerous "hydrophobicity scales" and "solvation parameters" have been proposed based on both theoretical considerations and  $\Delta G$  transfer measurements... Differences among such scales have fueled an active debate regarding which values, if any, are the ones that are relevant for protein folding, and led some to abandon the paradigm of hydrophobicity in favor of the more absolute concept of hydration

As noted in the utility guidelines (see: Federal Register, December 21, 1999, Volume 64, Number 244), basic research on a product to identify properties is an unsubstantial utility (see page 6 of the Utility guideline training materials). Therefore, Examiner maintains that the claims do not have substantial utility.

***Claim Rejections - 35 USC § 102 .***

4. Claims 1,3,6,22,24,27,33,35,38 are rejected under 35 U.S.C. 102(b) as anticipated by Cornette et al. (J. Mol. Biol., 1987,195,659-685).

The rejection is maintained for the reasons of record and further in view of the following.

Applicant argues that amendment of the claims to recite “to describe three-dimensional structure” overcomes the rejection. However, the amendment to the claims does not present any new method step limitation; rather, it recites an intended use of the method. However, an intended use limitations do not impart patentability of the claims where the method steps of the instant and referenced methods are the same.

5. Claims 1,3,6,22,24,27,33,35,38 are rejected under 35 U.S.C. 102(b) as anticipated by Eisenberg et al.

The rejection is maintained for the reasons of record and further in view of the following.

Applicant argues that that the reference does not teach shifting the hydrophobicity distribution. As addressed in the rejection, Eisenberg “normalized” hydrophobicity by averaging the normalized hydrophobicities for each residue over five scales, and by multiplying the result by standard deviation and adding it. Thus, the Eisenberg reference is viewed as reading on the instantly claimed method comprising steps of shifting hydrophobicity distribution based on a difference between values in the

hydrophobicity distribution and an average hydrophobicity value. As for applicant's references to the teaching in specification, the rejection addresses the method as described in the claims.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718. The fax phone



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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 Michael Borin, Ph.D.  
Primary Examiner  
Art Unit 1631

mlb  
03/23/2006